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## RESEARCH OF THE CHOICE OF THE BASIS OF A SEMI-SOLID MEDICINE WITH A SEMI-SOLID EXTRACT OF FEVERFEW (TANACETUM PARTHENIUM)

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**The aim.** To conduct the research on the choice of the basis for a mild drug with a semi-solid extract of feverfew for use in dermatology.

**Materials and methods.** In the study of the solubility of a semi-solid extract of feverfew (SSFE) used the method of optical microscopy using a laboratory microscope "Konus Academy". Determination of pH and homogeneity of the studied samples was performed according to the methods described in SPhU, Vol.1. The bioavailability of the model samples was investigated by diffusion in 3 % agar gel. Colloidal stability and thermal stability were determined according to the methods of GOST 29188.3-91. Measurements of rheological parameters were performed on a rotary viscometer "MYR 3000 V 2R" (Viskotech, Spain). Determination of particle distribution was performed using a laser diffraction analyzer of particle size Mastersizer 3000.

**Results.** The best results in determining the organoleptic properties, stability and degree of release of biologically active substances (BAS) showed samples prepared on emulgel and gel bases. Structural and mechanical parameters of the samples on these bases proved the presence of a non-Newtonian type of flow with plastic and thixotropic properties. When determining the distribution of SSFE particles by optical diffraction, their smaller size was determined in the sample on an emulgel basis in comparison with the gel.

**Conclusions.** Emulgel loaded with specific drugs has been found effective in some topical disorders, and it is emerging as potential drug delivery system in the area of dermatology. Since emu-lgel shows enhanced spreadability, adhesion, viscosity and extrusion. Based on the obtained results, an emulsion gel base was chosen as a carrier for a semi-solid drug with SSFE

**Keywords:** semi-solid dosage forms, semi-solid medicines, medicinal plants, Feverfew

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### 1. Introduction

Medicines created with the use of substances isolated from plant raw materials have been attracting attention for many decades. The Ukrainian market of herbal medicines is also characterized by a significant range. This is due to the fact that Ukraine has always been famous for the richness of the plant world and a serious scientific base, which has a huge potential of scientists and researchers in the field of medicine and pharmacy. It provides opportunities for the isolation of biologically active substances from medicinal plant raw materials in order to create on their basis modern domestic drugs.

In recent years, a number of scientific works by Ukrainian scientists have been devoted to the study of the chemical composition and pharmacological activity of little-studied medicinal plants. At the Department of Botany of National University of Pharmacy (NUPh), under the leadership of prof. Gontova T.M., obtained a semi-solid extract of feverfew (SSFE) of the Asteraceae family and confirmed a high content of phenolic substances in the classes of hydroxycinnamic acids, namely 3,5-dicafeoilouquine (1.575 %), 4,5-dicafeoilouquine (1.308 %) and chlorogenic (0.784 %) acid and sesquiterpene lactones. Among flavonoids, apigenin-7-glucoside (0.071 %) and kaempferol (0.041 %) were found [1, 2].

This spectrum of biologically active substances provides a pronounced anti-inflammatory, antibacterial

and analgesic effects, which was confirmed by pharmacological studies. In this regard, the creation of a new pharmaceutical drug of local action on the basis of SSFE is certainly promising [3, 4].

The leading place in the treatment of skin lesions is given to the means for external application in form of semi-solid medicines (SSM). SM based on plant extracts are widely used in medical practice for the treatment of various purulent-inflammatory, allergic and traumatic skin lesions.

The therapeutic effect of semi-solid medicines (semi-solid dosage forms) is significantly influenced by the type and nature of the bases, which are very diverse and tend to influence the release of active substances responsible for the desired therapeutic effect.

**In this regard, the aim of the research** was to choose a carrier base to create a drug in the form of a semi-solid dosage form (SSDF) with a semi-solid extract of feverfew, as an active pharmaceutical ingredient with anti-inflammatory, analgesic and antimicrobial properties.

### 2. Planning (methodology) of research

The development of semi-solid drugs is primarily not only in the search of effective APIs, but also in the selection of the optimal carrier base, which will ensure proper stability and pharmacological action.

The article contains a theoretical justification for the choice of active and scientific substantiation of excipients.

Research methods and the sequence of the experiment on the choice of carrier to create a drug in the form of a semi-solid dosage form:

- study of pharmaco-technological properties of the active pharmaceutical ingredient;
- choice of excipients based on literature data;
- development and research of the experimental samples.

### 3. Materials and methods

When choosing the optimal composition of the base of SSDF were used excipients approved for medical use.

For study of the solubility of SSFE as solvents were used purified water (20 and 60 degrees), 70 % ethyl alcohol and sunflower oil.

For selection of excipients of the base were used ointment bases of different types – emulsion, emulsion-gel and gel. The compositions of the bases included:

- solvents (purified water, sunflower oil);
- gel formers – Aristoflex AVC (Clariant, Switzerland), Sipimax ZEN (Seppic, France) [5];
- emulsifier-gelling agent – Sepiplus 400 (Seppic, France);
- emulsifiers – Prolipid 141 (O/W), Emulpharma PG20 (W/O) (Ashland, USA).

SSFE at a concentration of 1 % was added to the formulations of SSDF samples prepared on ointment bases of different types [5, 6]. The composition of the model samples is presented in Table 1.

Table 1

Compositions of the studied experimental samples

Type of ointment base, Excipients	Emulsion type o/w (I)	Emulsion type w/o (II)	Emul-gel (III)	Gel (IV)	Gel (V)	Gel (VI)
API:						
SSEF	1.0	1.0	1.0	1.0	1.0	1.0
EXCIPIENTS:						
Prolipid 141	6.0					
Emulpharma PG20		10.0				
Sepiplus-400			4.0	4.0		
Aristoflex AVC					2.0	
Sepimax ZEN						2.0
Sunflower oil	15.0	60.0	30.0			
Purified water	up to 100.0	up to 100.0	up to 100.0	up to 100.0	up to 100.0	up to 100.0

The **objects of the study** were model samples of the developed compositions. Their organoleptic, pharmaco-technological parameters and structural-mechanical (rheological) properties were studied in the obtained samples of ointment bases and in model samples of SSDF.

Optical microscopy was used to study the solubility of SSFE. The linear size and shape of the extract particles was determined using a laboratory microscope “Konus Academy”, using the method described in State Pharmacopoeia of Ukraine (SPhU) 2 ed., item 1.4. [7].

Determination of the **homogeneity** of the test samples with SSFE was performed according to the method described in SPhU 1.0, p. 511.

**Potentiometric determination of pH.** The pH level of the test samples was determined potentiometrically in accordance with the method of SPU 2.0, Volume 1, paragraph 2.2.3, p. 51–53. The device “pH-150 MI” was used in the work [7].

**Determination of colloidal stability.** (GOST 29188.3-91 “Cosmetic products. Methods for determining the stability of emulsions”). 2/3 tubes filled with the sample were placed in a water bath at a temperature of  $45 \pm 2$  °C for 20 min, then centrifuged for 5 min. at a speed of 6000 rpm. Stability was determined visually, in the presence of stratification – not stable, without changes – stable.

**Determination of bioavailability** by agar diffusion was performed as follows: prepared 3 % agar gel

with the addition of iron (III) chloride was poured into Petri dishes, and the degree of release of the substance was recorded after 24 hours on the radius of the colored area.

Measurements of **rheological parameters** of model samples of bases were performed on a rotary viscometer “MYR 3000 V2R” (Viscotech, Spain) in a system of coaxial cylinders according to the method of the State Pharmacopoeia of Ukraine (SPhU 2.0, Volume 1, paragraph 2.2.10, p. 58–59) in a wide range of shear rates. The study was performed at a temperature of  $(20 \pm 0.1)$  °C. Based on the measurement results, rheograms of the dependence of the shear stress ( $\tau$ ) on the shear rate gradient ( $Dr$ ) and the viscosity on the shear stress at a speed of 1.0 to 200 rpm were constructed.

To determine the **particle distribution** of SSFE in model samples of SSDF, the method of laser diffraction was used, which is based on the phenomenon of light scattering by particles in all directions: there is a diffraction pattern of intensity distribution, which depends on particle size. The study was performed using a laser diffraction analyzer of particle size Mastersizer 3000, operating in the range of 0.01 – 3500  $\mu\text{m}$  [8].

**Thermal stability** studied in a thermostat brand TC-80 MG with a temperature of  $(42.5 \pm 2.5)$  °C for 7 days. Stability is determined visually according to (GOST 29188.3-91 “Cosmetic products. Methods for determining the stability of the emulsion”).

**4. Results**

The first stage of our research on the choice of base for SSDF under development was the study of the solubility of SSFE, aimed at determining the rational way of introducing API into the base and providing the necessary biopharmaceutical requirements, the main of which is the rapid and complete release of active substances [9].

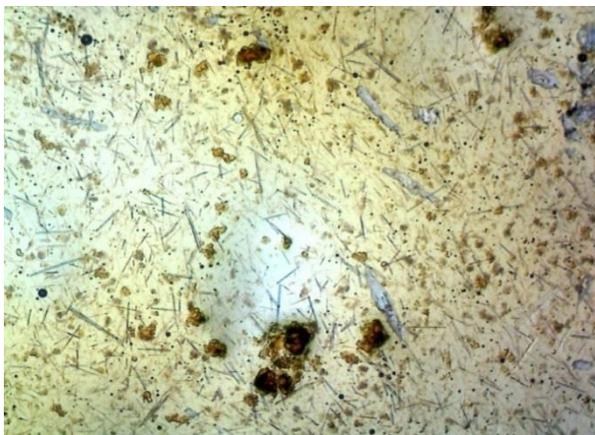


Fig. 1. Photomicrograph of a semi-solid extract of feverfew

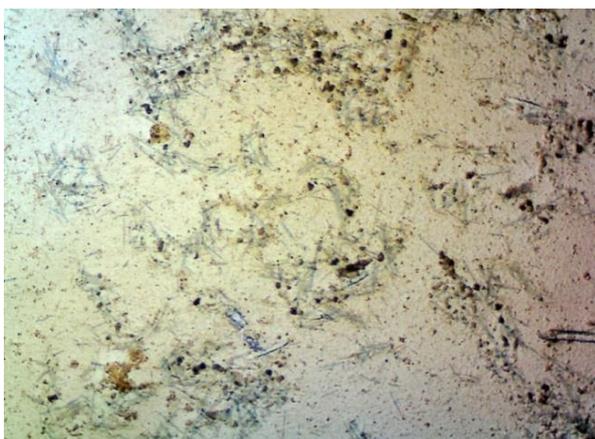


Fig. 2. Micrograph of SSFE with 70 % ethyl alcohol in a ratio of 1:1

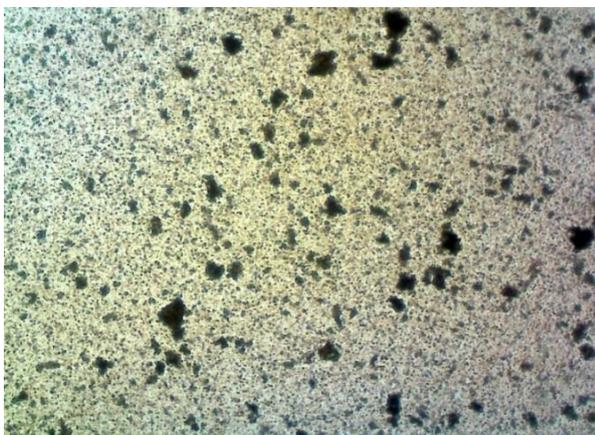


Fig. 3. Micrograph of SSFE with purified water in a ratio of 1:1 (t 20±2 °C)

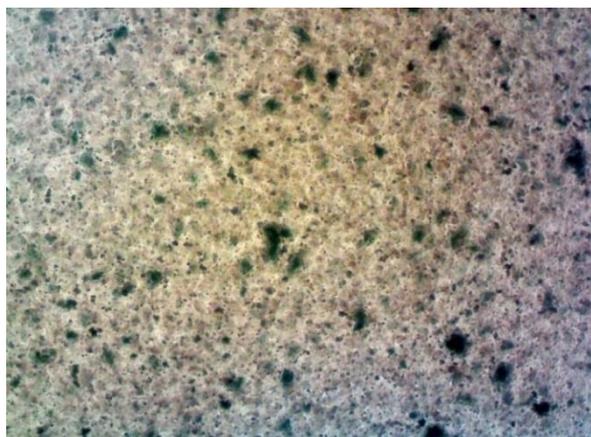
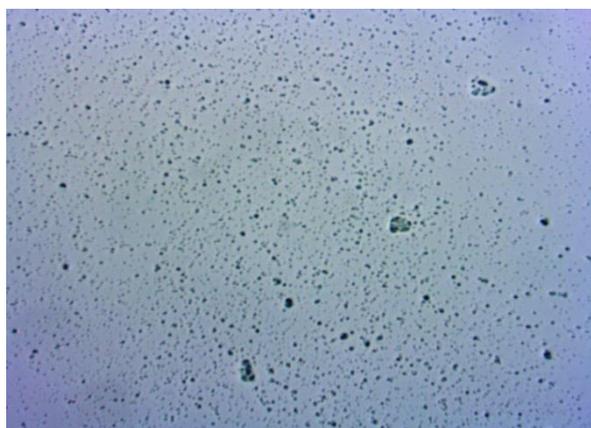


Fig. 4. Micrograph of SSFE with purified water in a ratio of 1:1 (t 60±2 °C)



*a*



*b*

Fig. 5. Micrograph of SSFE with purified water in the ratio: *a* – 1: 5 (t 20±2 °C); *b* – 1:10 (t 20±2 °C)

The results of determining the quality indicators of the model samples are given in Table 2.

All samples show pseudoplastic behavior, in which their viscosity decreases with increasing stress (Fig. 8).

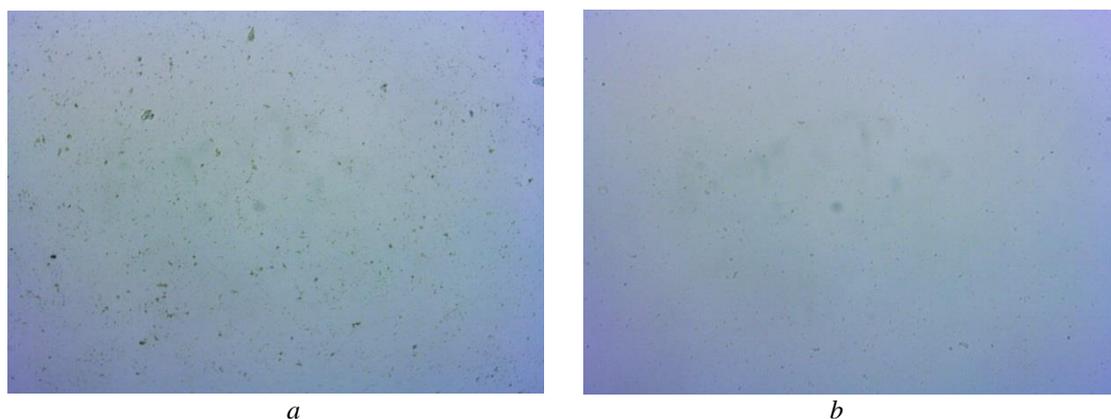


Fig. 6. Micrograph of SSFE with purified water in the ratio: *a* – 1:30 ( $t 20 \pm 2$  °C); *b* – 1:100 ( $t 20 \pm 2$  °C)

Table 2

## Organoleptic and physicochemical properties of model samples

No.	Organoleptic indicators	Colloidal stability	Thermal stability	pH	Structural viscosity, mPa·s (20/200 rpm at 20 °C)	Penetration into agar gel, mm
1	Stratification of the sample is observed, inhomogeneous consistency is determined.	Not stable	Not stable	5.0±0.09	450/120	–
2	Stratification of the sample is observed, inhomogeneous consistency is determined.	Not stable	Not stable	4.9±0.11	505/170	–
3	Mass of homogeneous consistency, without visible inclusions, pale yellow with a white tinge with a specific pleasant odor. The texture is not dense.	Stable	Stable	5.6±0.09	2000/600	22±0.07
4	Mass of uniform consistency, without visible inclusions, pale yellow with a white tinge, shiny surface with a specific pleasant odor. The texture of the sample is dense, evenly distributed on the skin.	Stable	Stable	5.6±0.06	15400/4450	19±0.05
5	Sample of uniform consistency, without visible inclusions, yellow-brown color, shiny surface. The texture of the sample is dense, evenly distributed on the surface of the skin, does not leave a feeling of stickiness.	Stable	Stable	5.5±0.07	29000/4500	16±0.03
6	Sample of uniform consistency and color (yellow-brown) with air bubbles. The smell is specific, pleasant. The texture is viscous, dense. Evenly distributed on the skin, leaves a slight feeling of stickiness to complete absorption.	Stable	Stable	5.5±0.06	16700/2600	17±0.06

Note: \* –  $n=3$

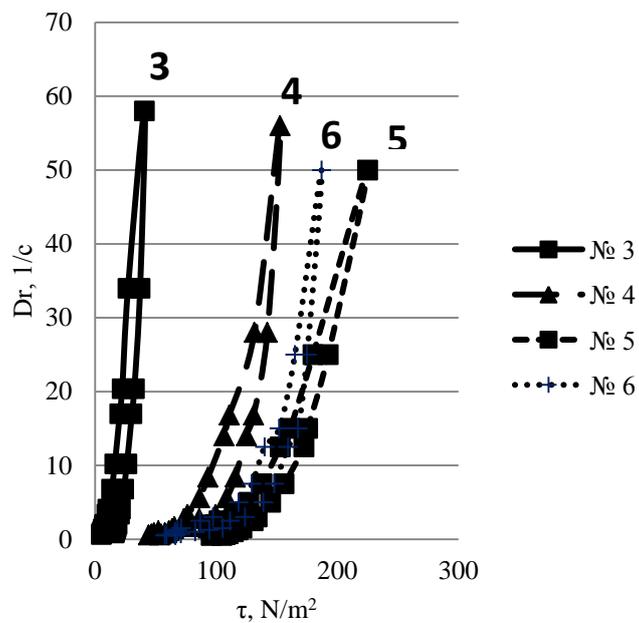


Fig. 7. Rheogram of the tested samples

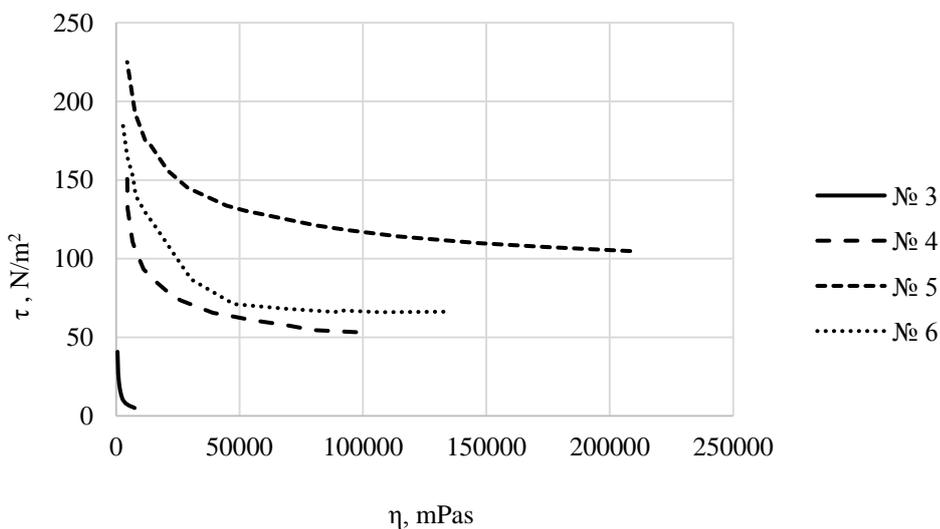


Fig. 8. Dependence of erosion viscosity on the suspension stress

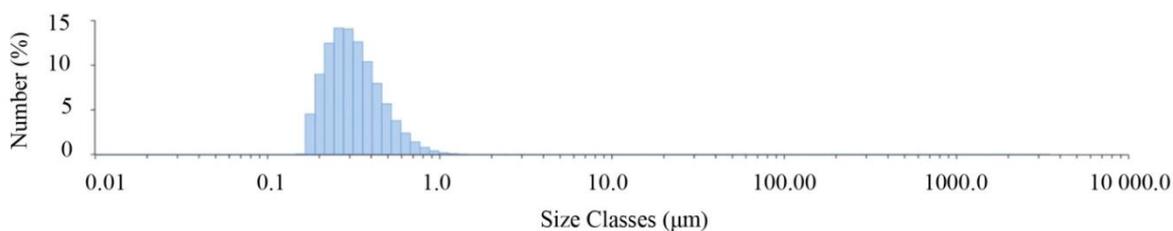


Fig. 9. Particle size distribution of the extract based on emulgel, sample No. 3

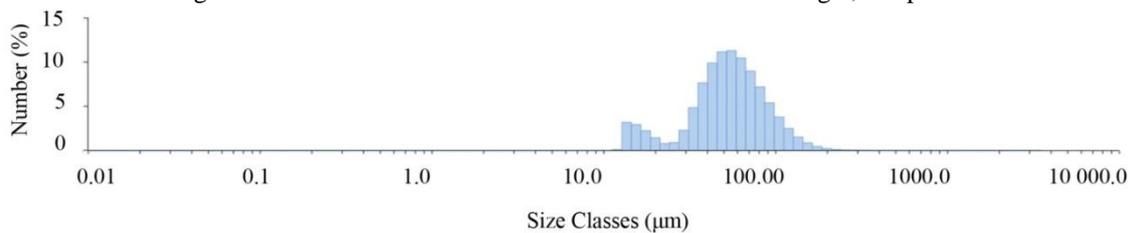


Fig. 10. Distribution of extract particles by size in the gel base, sample No. 4

Table 3

Distribution of extract particles by size

No.	Particle size, (µm)	Amount, %	
		Sample No. 3	Sample No. 4
1.	0.146	0.05	
2.	0.166	4.53	
3.	0.188	8.98	
4.	0.214	12.47	
5.	0.243	14.16	
6.	0.276	14.07	
7.	0.314	12.62	
8.	0.357	10.4	
9.	0.405	7.95	
10.	0.46	5.67	
11.	0.523	3.79	
12.	0.594	2.38	
13.	0.675	1.41	
14.	0.767	0.78	
15.	0.872	0.4	
16.	0.991	0.19	
17.	1.13	0.08	
18.	1.28	0.02	
19.	11.2		0.09
20.	12.7		3.17
21.	14.5		2.91
22.	16.4		2.22
23.	18.7		1.43
24.	21.2		0.77
25.	24.1		0.88
26.	27.4		2.28
27.	31.1		4.83
28.	35.3		7.64
29.	40.1		9.9
30.	45.6		11.16
31.	51.8		11.29
32.	58.9		10.47
33.	66.9		8.99
34.	76		7.19
35.	86.4		5.38
36.	98.1		3.77
37.	111		2.47
38.	127		1.5
39.	144		0.85
40.	163		0.44
41.	186		0.21
42.	211		0.09
43.	240		0.04
44.	272		0.02
45.	310		0.01

### 5. Discussion

To study solubility of the semi-solid extract in solvents used in the pharmaceutical industry: in purified water, 70 % ethanol and sunflower oil. The solutions were prepared in a ratio of 1:1.

The main characteristics of microscopic examination are the shape of the particles, their size, color and fractional composition. The factor forms as the ratio of the width and length of the particles.

As we can see from Fig. 1, SSFE contains three groups of particles of different shapes. The first is a needle, transparent particles with a length of 0.1 to 1.5 µm with a shape coefficient of 0.01–0.1. The second group for several groups is agglomerates of brown prismatic particles (0.2–1.5 µm), shape factor 0.85–0.95.

The third is bulk particles of indeterminate white shape with jagged edges, 0.2–2.0 µm long, shape factor 0.2–0.3.

When sunflower oil was added to the extract, a sticky mass is created, which does not have a uniform distribution in the microscope field.

The addition of 70 % ethyl alcohol (1:1) to SSFE reduced the linear size of the needle particles by an average of 5 times, their size became no more than 0.2  $\mu\text{m}$ , the form factor – 0.1–0.2 (Fig. 2). Also in the field of view, a uniform distribution of prismatic particles with a size of 0.2–0.5  $\mu\text{m}$  was observed. The three-dimensional white particles completely dissolved.

Addition to SSFE of purified water with a temperature of  $20 \pm 2$  °C (Fig. 3) in a ratio of 1:1 led to the complete disappearance of needle particles and three-dimensional white particles of indeterminate white color from the field of view, as well as a significant reduction in the linear size of prismatic particles.

With increasing water temperature, there was a change in the shape and size of the particles, which indicates their partial dissolution.

In both samples, purified water showed significant limiting wetting of prismatic particles, followed by swelling limitation (Fig. 3–4).

When the amount of solvent increased to a ratio of 1:5 and 1:10, a change in the shape of the particles and a decrease in their size was observed (Fig. 5).

When the amount of solvent was increased to 1:30 and 1:100, there was a further decrease in the number of extract particles in the field of view (Fig. 6).

According to the results of the study it was found that the use of any of the selected solvents did not lead to complete dissolution of all components of the analyzed extract, which can be explained by the presence of different chemical structure and, accordingly, physicochemical properties. The best distribution of SSFE was observed in ethyl alcohol and purified water. However, due to the possible irritating effect of ethyl alcohol on the skin when used in SSDF, it was excluded from further studies. Increasing the amount of purified water in the range from 1:30 to 1:100 led to a decrease in SSFE particles with optimal size and shape [9].

The emulsion, gel-emulsion and gel bases were used for the study and further development of SSDF with a semi-solid extract of dark burgundy, to which was added 1 % SSFE, which was administered in a water-dispersed purified form. The ratio of extract and solvent in the test samples depended on the composition of the test sample and ranged from 1:30 to 1:95. The development of emulsion carrier bases involves the choice of an optimal ratio of oil and water phases, as well as the nature and concentration of emulsifiers.

An important task is to ensure the stability of the SSDF, which can be solved by selecting complex emulsifiers of the 1st and 2nd type, the introduction of emulsions of thickener stabilizers and others.

Thus, various modern emulsifiers, emulsifiers-gelling agents and for hydrophilic gel structures – modern gelling agents, which are currently most often used in scientific research, were used to create stable model emulsion systems. Concentrations of excipients were selected based on the analysis of the results of special literature sources [5–7].

As can be seen from the Tab. 1, sample No. 1 – emulsion system of type o/w; sample No. 2 – emulsion system type w/o; sample No. 3 – emulsion system type w/o/w with emulsifier – gelling agent; samples No. 4, 5 and 6 are represented by hydrophilic bases – gels.

Prepared samples on different carrier bases with 1 % SSFE were evaluated for organoleptic and consumer properties, their colloidal and thermal stability, structural viscosity, pH, size and distribution of individual particles and the degree of penetration of API (release) into agar were studied [7, 8].

As can be seen from data tables 2, samples No. 1 and No. 2, prepared on emulsion bases o/w and w/o, according to small independent organs of organoleptic parameters (inhomogeneous consistency and color, staining with precipitation), do not meet the criteria of colloidal and urgent stability, in addition, there was no release of flavonoid nature in agar gel, so they were included in further studies.

Samples No. 3–6 had good organoleptic properties, were stable and had a satisfactory pH value.

To study the dynamics of the release of phenolic compounds in to agar was added a specific reagent ( $\text{FeCl}_3$ ), capable of interacting with the active substance to give a color reaction.

The diffusion of phenolic active compounds in agar was used to determine the degree and observe the rate and dynamics of release from the test samples. According to the degree of release of BAS, the samples can be placed in the following sequence: 3>4>6>5.

Therefore, the next step was to study the structural and mechanical properties of samples 3–6. The results of the study of the main rheological parameters of the studied samples are presented in Fig. 7, 8.

It was found that all samples have a non-Newtonian type of flow, in which the viscosity  $\eta$  ( $\gamma$ ) and the coefficients of normal stresses  $\psi_1$  ( $\gamma$ ),  $\psi_2$  ( $\gamma$ ) depend on the shear rate. When graphically depicting these processes in Fig. 7 “downward curve” differs from the “upward curve” with the formation of a hysteresis loop, due to the preservation of residual deformation after strong weakening of the structure under the influence of previously applied stress, and indicates that all test samples have certain thixotropic properties [10, 11].

The constructed curves of the studied samples No. 4–6 show the flow not immediately, but only after the applied voltage required to break the structural elements. Under the influence of high shear stresses, the structure of the gels is destroyed, and when the shear stress is removed, their structural viscosity is restored. In contrast to gel samples, the flow of emulgel sample No. 3 began faster (Fig. 7).

During the voltage drop, the viscosity of all samples is gradually restored, which confirms the thixotropic properties of the studied samples. An increase in the viscosity of the samples was observed in the series No. 3<No. 4<No. 6<No. 5 (Fig. 8).

That is, the smallest input medium of wet emitters based on emulsion-gel, samples based on gelling substances Sepimax ZEN and Sepiplus-400 provide the closest values as expansion, and the largest due to

the creation of fiber solutions based on Aristoflex AVC.

Thus, samples of experiments 3 and 4 were selected for further studies, which showed satisfactory results of previous tests. In these samples, the particle size distribution of the extract was investigated by laser diffraction. The research results are presented on Fig. 9, 10 and in table 3 [12, 13].

As can be seen from Fig. 9, sample No. 3 contains particles with a size of 0.146 to 1.28 nm with a maximum content of particles with a size of 0.243 nm – 14.16 %. Sample No. 4 (Fig. 10) contains particles ranging in size from 11.2 to 310 nm with a maximum content of 51.8 nm – 11.29 % [14, 15].

Thus, the smaller particle size of SSFE and a narrower range of their size distribution is observed in the sample No. 3, prepared on an emulgel basis (Fig. 9). The above confirms the results of studies on obtaining better values for the release of BAS (and, of course, their greater bioavailability when used) with SSDF in the form of emulgel [16].

After analyzing and substantiating the results of the above studies, an emulsion gel base was used using the emulsifier-gelling agent Sepiplus-400 and sunflower oil for the preparation of SSDF, where SSFE is in a water-dispersed purified form.

**Study limitations.** The conducted research on the development of the technology of a semi-solid dosage form in laboratory conditions does not fully reflect the possible risks of obtaining this dosage form in industrial.

**Prospects for the further research.** A promising direction for further research is the development of the final composition of a new original drug for use in der-

matology, pharmacological research, development of technological regulatory documentation for its production, verification of the compliance of the developed drug with quality parameters, as well as justification of the technological process.

## 6. Conclusions

1. Based on the determination of the solubility of SSFE, it was found that the best distribution of its particles is observed in purified water. Therefore, it is proposed to introduce it into the composition of SSDF in water-dispersed purified form.

2. When determining the organoleptic properties of model samples prepared on emulsions, emulsions-gels and gel bases, it was found that samples prepared on emulsion bases of type o/w and w/o had unsatisfactory organoleptic characteristics and did not emit flavonoid BAS. Samples based on emulgel and gel had good organoleptic properties, the required stability and a sufficient degree of BAS release.

3. Based on the study of rheological parameters, it was found that the above prototypes belong to structured systems, have a satisfactory consistency and thixotropic properties.

4. The results of determining the distribution of SSFE particles by optical diffraction showed a smaller particle size in the sample based on emulgel (from 0.15 to 1.3  $\mu\text{m}$ ) compared to the sample based on gel (from 11 to 310  $\mu\text{m}$ ), which was also taken into account when choosing emulgel bases with SSFE (sample No. 3).

## Conflict of interests

The authors declare that they have no conflicts of interest.

## References

1. Hordiei, K. R., Gontova, T. M., Serbin, A. G., Kotov, A. G., Kotova, E. E. (2019). Study of phenolic compounds in the Feverfew Herb by TLC and HPLC methods. *Ukrainian biopharmaceutical journal*, 3 (60), 64–70. doi: <http://doi.org/10.24959/ubphj.19.225>
2. Sur, R., Martin, K., Liebel, F., Lyte, P., Shapiro, S., Southall, M. (2008). Anti-Inflammatory Activity of Parthenolide-Depleted Feverfew (*Tanacetum parthenium*). *Inflammopharmacology*, 17 (1), 42–49. doi: <http://doi.org/10.1007/s10787-008-8040-9>
3. Konovalova, D. S., Konovalov, D. A. (2008). Seskviterpenovye laktony piretruma devichego kak biologicheski aktivnye veschestva (obzor). *Ekologiya cheloveka*, 3, 3–7.
4. Pareek, A., Suthar, M., Rathore, G., Bansal, V. (2011). Feverfew (*Tanacetum parthenium* L.): A systematic review. *Pharmacognosy Reviews*, 5 (9), 103–110. doi: <http://doi.org/10.4103/0973-7847.79105>
5. Ruban, O. A., Pertsev, I. M., Kutsenko, S. A., Maslii, Yu. S.; Pertsev, I. M. (Ed.) (2016). *Dopomizhni rechovyny u vyrobnytstvi likiv*. Kharkiv: Zoloti storinky, 720.
6. Rowe, R. C., Sheskey, P. J., Cook, W. G., Fenton, M. E. (Eds.) (2012). *Handbook of Pharmaceutical Excipients*. London: Pharmaceutical Press, 1064.
7. *Derzhavna farmakopeia Ukrainy*. Vol. 1. (2015). Kharkiv: Derzhavne pidpriemstvo «Ukrainskyi naukovi farmakopeinyi tsentr yakosti likarskykh zasobiv», 1128.
8. *European Pharmacopoeia* (2016). European Directorate for the Quality of Medicines (EDQM). Strasbourg: Council of Europe, 4016.
9. Velia, M. I., Khalavka, M. V., Ruban, O. A. (2019). Vyznachennia rozchynnosti hustoho ekstraktu maruny divochoi (*Tanacetum parthenium* (Feverfew)) mikroskopichnym metodom. *Tekhnolohichni ta biofarmatsevtichni aspekty stvorennia likarskykh preparativ riznoi napravlenosti dii*. Kharkiv: Vyd-vo NFau, 58–61.
10. Lauterbach, A., Müller-Goymann, C. C. (2014). Comparison of rheological properties, follicular penetration, drug release, and permeation behavior of a novel topical drug delivery system and a conventional cream. *European Journal of Pharmaceutics and Biopharmaceutics*, 88 (3), 614–624. doi: <http://doi.org/10.1016/j.ejpb.2014.10.001>
11. Kulkarni, V. S., Shaw, C. (2016). Particle Size Analysis: An Overview of Commonly Applied Methods for Drug Materials and Products. *Essential Chemistry for Formulators of Semisolid and Liquid Dosages*, 137–144. doi: <http://doi.org/10.1016/b978-0-12-801024-2.00008-x>
12. Dhamoon, R., Popli, H., Aggarwal, G., Gupta, M. (2018). Particle Size Characterization- Techniques, Factors and Quality-by-design Approach. *International Journal of Drug Delivery*, 10, 1–11.

13. Dhawas, V., Dhabarde, D., Patil, S. (2020). Emulgel: A Comprehensive Review for Novel Topical Drug Delivery System. International Journal of Recent Scientific Research, 11 (4), 38134–38138.
14. Sahu, T., Patel, T., Sahu, S., Gidwani, B. (2016). Skin cream as topical drug delivery system: a review. Journal of Pharmaceutical and Biological Sciences, 4 (5), 149–154.
15. Sharadha M, Gowda D V, Vishal Gupta N, Akhila A R. (2020). An overview on topical drug delivery system – Updated review. International Journal of Research in Pharmaceutical Sciences, 11 (1), 368–385. doi: <http://doi.org/10.26452/ijrps.v11i1.1831>
16. Tanaji, D. N. (2018). Emulgel: A Comprehensive Review for Topical Delivery of Hydrophobic Drugs. Asian Journal of Pharmaceutics, 12 (2), 382–393. doi: <http://doi.org/10.22377/ajp.v12i02.2366>

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